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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/016,737	MURPHY ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-37* is/are pending in the application.

4a) Of the above claim(s) *25 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,26 and 28-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 23-24, 26, 28-37 are being examined.

Declaration

Applicant submits the Declaration by Dr. Alton Boynton, stating that the conception and reduction to practice of the claimed invention is prior to the January 27, 1995 date of Cohen et al.

The submission of the Declaration by Dr. Alton Boynton is acknowledged and entered.

New Rejections Based on New Consideration

Claim Objections

Claim 37 is objected to, for the use of the language "the a recipient".

For the purpose of compact prosecution, it is assumed that claim 37 is drawn to the composition of claim 36, wherein the dendritic cells are HLA-matched for a recipient.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 23, 31-32, 33-37 are rejected under 35 USC 103(a) as being obvious over Sallusto et al, 1994 (J Exp Med, 179: 1109-1118, of record), in view of Bigotti G et al, 1991 (Prostate, V19, N1, p.73-87), as evidenced by Inaba K et al, 1987 (Journal of experimental medicine (UNITED STATES), 166 (1) p:182-94, of record).

Claim 23 is drawn to: A composition comprising an isolated cell population having human dendritic cells, that has been cultured in the presence of granulocyte- macrophage colony-stimulating factor (GM-CSF), and interleukin-4 (IL-4), and exposed *in vitro* to a soluble prostate antigen. The cell population has an increased ability to activate T cells specific to the prostate antigen, as compared to a cell population cultured in the presence of granulocyte- macrophage colony-stimulating factor, interleukin-4, that has not been exposed *in vitro* to the prostate antigen.

Claim 31 is drawn to: The composition of claim 23, wherein the cell population has an increased ability to activate T cells specific to the prostate antigen, 2 to 3 fold more as compared to a cell population cultured in the presence of granulocyte- macrophage colony-stimulating factor, interleukin-4, that has not been exposed *in vitro* to the prostate antigen.

Claim 32 is drawn to: The composition of claim 23, wherein the dendritic cells are immature dendritic cells.

Claims 33-34 are drawn to: The method of claim 23, wherein the T cells are CD4+ or CD8+.

Claims 35-36 are drawn to: The composition of claim 23, wherein the dendritic cells are isolated from a prostate cancer patient (claim 35) or a normal individual (claim 36).

Claim 37 is drawn to: The composition of claim 36, wherein the dendritic cells are HLA-matched for a recipient.

Sallusto et al teach that the exposure to GM-CSF plus IL- 4 converts blood mononuclear cells to immature dendritic cells, that maintain the antigen capturing and processing capacity characteristics of immature dendritic cells *in vivo* and efficiently present soluble antigen, such as tetanus toxoid to specific T cell clones (abstract). Sallusto et al teach that dendritic cells (DCs) exist in two stages of maturation. Sallusto et al teach that as immature dendritic cells, they are capable of antigen capture/processing and immunostimulation, but as they mature, they lose antigen-capturing capacity (p.1109). Sallusto et al teach that Langerhans cells represent immature dendritic cells in skin (p.1109, first column, first two lines of second paragraph). Sallusto et al teach that the dendritic cells are from human peripheral blood (p.1110, first column, line 6 of second paragraph).

Sallusto et al do not teach that the antigen is a prostate antigen. Sallusto et al do not teach that the activation of T cells specific for prostate antigen is 2 to 3 fold more than that of the control.

Bigotti et al teach that Langerhans cells, a type of dendritic cells, are capable of direct prostate antigen presentation to immune cells, and eliciting the immune response, providing a means for controlling the escape of cancer cells from the immune surveillance (abstract, p. 85). Bigotti et al teach that Langerhans cells are found mainly in low grade prostate cancer, as opposed to the higher grades, and represent a good prognostic indicater (abstract). Bigotti et al teach that the number of Langerhans cells is directly correlated with the expression of HLA class II-DR molecules of tumor cells, and that Langerhans cells and HLA class II molecule provide a

means of eliciting the immune response. Bigotti et al teach that it is commonly believed that the antigen presenting properties are dependent upon HLA class II expression (p.74, 4th paragraph).

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to obtain human, immature dendritic cells, using the method taught by Sallusto et al, and to replace the antigen tetanus toxoid taught by Sallusto et al with a prostate antigen taught by Bigotti et al, for exposure of the prostate antigen to the immature dendritic cells, because the dendritic cells, such as Langherhans' cells, would present prostate antigen to immune cells, and activate specific immune response, and thus, would provide treatment of prostate cancer.

Moreover, one would have a reasonably expectation of success, because the immature dendritic cells, obtained from culture in GM-CSF and interleukin-4, maintain the antigen capturing and processing capacity characteristics of immature dendritic cells *in vivo,* and efficiently present soluble antigen, as taught by Sallusto et al, and because Langerhans cells, which are a type of dendritic cells, are found mainly in low grade prostate cancer, as opposed to the higher grades, and represent a good prognostic indicater, and further because the Langerhans cells are capable of direct prostate antigen presentation to immune cells, and eliciting the immune response, as taught by Bigotti et al.

In addition, it would have been obvious to obtain blood mononuclear cells from a prostate cancer patient for converting to immature dendritic cells, because the dendritic cells from the prostate cancer patient would be readily available, and would not require donor blood mononuclear cells, and because one would have expected that blood mononuclear cells from a

prostate cancer patient would also be able to be converted to immature dendritic cells, using the method taught by Sallusto et al.

Further, it would have been obvious to match the dendritic cells isolated from a normal individual with HLA of the recipient, because dendritic cells, such as Langerhans cells, are directly correlated with HLA class, as taught by Bigotti et al, and thus would not present the antigen with non-matched HLA cells.

Although the references do not explicitly teach that the dendritic cells can activate 2 to 3 fold more T cells specific to the prostate antigen as compared to a cell population cultured in the presence of granulocyte- macrophage colony-stimulating factor, interleukin-4, that has not been exposed *in vitro* to the prostate antigen, however, it is noted that the immature dendritic cells taught by Sallusto et al, after exposure to a prostate antigen, would present the prostate antigen, and be able to activate 2 to 3 fold more T cells specific to the prostate antigen, because the immature dendritic cells taught by Sallusto et al are produced by the same process as disclosed in the specification of the instant invention, i.e. cultured in the presence of GM-CSF and IL-4. The claimed dendritic cells appear to be the same as the dendritic cells taught by the combined art, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

It is noted that the dendritic cells taught by Sallusto et al, Bigotti G et al, and Stites DP would activate CD4+ and/or CD8+ T cells , because activation of CD4+ and/or CD8+ T cells is a property of dendritic cells, as evidenced by Inaba K et al. Further, although the references do not specifically teach that the dendritic cells activate CD4+ and/or CD8+ T cells, however, the claimed dendritic cells appear to be the same as the dendritic cells taught by the combined art, supra, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

It is further noted that although Sallusto et al do not explicitly state that the human peripheral blood is from a normal individual, Sallusto et al do not state that the human peripheral blood is from a diseased individual; and the human peripheral blood taught by Sallusto et al would be expected to be from a normal donor individual.

2. Claim 24 is rejected under 35 USC 103(a) as being obvious over Sallusto et al, in view of Bigotti G et al, and as evidenced by Inaba et al, supra, and further in view of Cohen, PA et al, 1994 (Cancer Research, 54(4): 1055-8).

Claim 24 is drawn to the composition of claim 23, in which the prostate antigen is a lysate of prostate tumor cells.

The teaching of Sallusto et al, Bigotti G et al, and Inaba et al has been set forth above.

Sallusto et al, Bigotti G et al, and Inaba et al do not teach that the antigen is a lysate of prostate tumor cells.

Cohen et al teach that syngeneic dendritic cells, when pulsed with tumor lysate, induces antigen-specific proliferation of antitumor CD4+ T cells, relevant to the rejection of the syngenic methylcholanthrene tumor (abstract).

It would have been obvious to use as prostate antigen, a lysate of prostate cancer cells from a prostate cancer patient, because prostate cancer cells would have several prostate cancer-specific antigens, and because a tumor lysate successfully primes the dendritic cells for inducing antigen-specific proliferation of antitumor CD4+ T cells, as taught by Cohen et al, and further because using tumor lysate would be more convenient, and does not require the extra step of purification of the antigen.

3. Claim 26 is rejected under 35 USC 103(a) as being obvious by Sallusto et al, in view of Bigotti et al, and as evidenced by Inaba et al, supra, as applied to claim 23, and further in view of Lutz et al (of record).

Claim 26 is drawn to the composition of claim 23, wherein the dendritic cells are extended life span dendritic cells.

The teaching of Sallusto et al, Bigotti et al, and Inaba has been set forth above.

Sallusto et al, Bigotti et al and Inaba et al do not teach that the dendritic cells are extended life span dendritic cells.

Luz et al teach making immortalized dendritic cells (Abstract), which overcomes the problem of being unable to maintain dendritic cells *in vitro* for long periods of time (p.278).

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to immortalize the dendritic cells taught by Sallusto et al, Bigotti et al, and Inaba et al, using the immortalizing method taught by Luz et al, because immortalizing dendritic cells would enable maintainance of dendritic cells *in vitro* for long periods of time, as taught by Luz et al.

4. Claims 28-29 are rejected under 35 USC 103 as being obvious by Sallusto et al, Bigotti et al, Inaba et al, and Cohen et al, supra, as applied to claim 23, and further in view of Taylor et al (of record).

Claim 28 is drawn to the composition of claim 23, wherein the dendritic cells have been cryopreserved prior to exposure *in vitro* to the prostate antigen, and wherein said dendritic cells retain the abililty to take up and present antigen.

Claim 29 is drawn to the composition of claim 28, wherein the prostate antigen is a lysate of prostate tumor cells.

The teaching of Sallusto et al, Bigotti et al, Inaba et al and Cohen et al has been set forth above.

Sallusto et al, Bigotti et al, Inaba et al, and Cohen et al do not teach that the dendritic cells are cryopreserved..

Taylor et al teach cryopreservation of dendritic cells, wherein said cryopreserved dendritic cells can be used in immunological procedures.

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to cryopreserve the dendritic cells taught by Sallusto et al, Bigotti et al,

Stites, and Cohen et al, using the cryopreservation method taught by Taylor et al, to preserve the previously isolated dendritic cells for later use.

5. Claim 30 is rejected under 35 USC 103 as being obvious by by Sallusto et al, Bigotti et al, and Inaba et al, supra, as applied to claim 23, and further in view of Taylor et al (of record), as applied to claim 28, and Lutz et al, of record.

Claim 30 is drawn to a composition of claim 28, wherein the dendritic cells are extended life dendritic cells.

The teaching of Sallusto et al, Bigotti et al, Inaba et al and Taylor et al has been set forth above.

Sallusto et al, Bigotti et al, Inaba et al and Taylor et al do not teach that the dendritic cells have extended life.

Luz et al teach making immortalized dendritic cells (Abstract), which overcomes the problem of being unable to maintain dendritic cells *in vitro* for long periods of time (p.278).

It would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to immortalize the cryopreserved dendritic cells taught by Sallusto et al, Bigotti et al, Inaba et al and Taylor et al, using the immortalizing method taught by Luz et al, because immortalizing dendritic cells would allow maintainance of dendritic cells *in vitro* for long periods of time, as taught by Luz et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

MINH TAM DAVIS

April 21, 2006